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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/815,341	03/22/2001	Nancy J. Bump	BBC-069	4413

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EXAMINER	
SMITH, CAROLYN L	
ART UNIT	PAPER NUMBER
1631	

MAIL DATE	DELIVERY MODE
07/02/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	09/815,341	BUMP ET AL.	
	Examiner	Art Unit	
	Carolyn L. Smith	1631	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on *30 April 2007*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-88* is/are pending in the application.

4a) Of the above claim(s) *1-20, 28-31,34-88* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *21-27,32 and 33* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Applicant's amendments and remarks, filed 4/30/07, are acknowledged.

Applicant's arguments, filed 4/30/07, have been fully considered but they are not deemed to be persuasive. Rejections and/or objections not reiterated from the previous office actions are hereby withdrawn. The following rejections and/or objections are either reiterated or newly applied. They constitute the complete set presently being applied to the instant application.

Claims 1-20 and 36-88 remain withdrawn as being drawn to non-elected Groups. Claims 28-31, 34, and 35 remain withdrawn as being drawn to non-elected species.

Claims herein under examination are 21-27, 32, and 33.

Claims Rejected Under 35 U.S.C. § 112 1st Paragraph

The following is a quotation of the first paragraph of 35 U.S.C. § 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Factors to be considered in determining whether a disclosure would require undue experimentation have been summarized in Ex parte Forman, 230 USPQ 546 (BPAI 1986) and reiterated by the Court of Appeals in In re Wands, 8 USPQ2d 1400 at 1404 (CAFC 1988). The factors to be considered in determining whether undue experimentation is required include: (1) the quantity of experimentation necessary, (2) the amount or direction presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6)

the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims. The Board also stated that although the level of skill in molecular biology is high, the results of experiments in genetic engineering are unpredictable. While all of these factors are considered, a sufficient amount for a *prima facie* case are discussed below.

LACK OF ENABLEMENT

Claims 21-27, 32, and 33 are rejected under 35 U.S.C. § 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

This rejection is maintained.

Claim 21 is directed to identifying a compound that is an inhibitor of a Tie-2 protein by crystallizing the protein, obtaining atomic coordinates, using the atomic coordinates to define the active subsites, identifying a compound that binds to one or more active subsites, *wherein the compound which binds to the active subsite or sites is an inhibitor of a Tie-2 protein.* How does one skilled in the art determine if a compound is an inhibitor merely by determining if it fits into an active site? One skilled in the art would not conclude that a compound that binds to an "active subsite or sites" of Tie-2 is necessarily an inhibitor, since this compound could equally be an activator (agonist) or have no effect, depending on where and how it binds. One skilled in the art would need to have additional information, such as information regarding which residues of the protein interact with known inhibitors or some other comparison of binding properties to known inhibitors. The need for this additional information demonstrates that further experimentation/information would be necessary to determine if an inhibitor has actually been

identified. Because of the experimentation necessary, the unpredictability of knowing whether a compound inhibits, activates, or has no effect on a protein due to its binding ability to one or more active subsite(s) on a protein, and the breadth of the claims, there is a lack of enablement. Claims 22-27, 32, and 33 are also rejected due to their dependency from claim 21.

Applicants reiterate the Examiner's question of how does one skilled in the art determine if a compound is an inhibitor merely by determining if it fits into an active site. Applicants direct attention to the following passages of the specification:

> 1) Page 4, line 24 to page 5, line 3 wherein Applicants teach how the methods of the invention can be used to facilitate formation of Tie-2 crystals which enable the rational development of inhibitors of Tie-2.
> 2) Page 5, line 25 to page 6, line 2 wherein Applicants teach using the atomic coordinates derived from study of polypeptides comprising the catalytic domain of Tie-2 to identify compounds that fit in the catalytic domain.
> 3) Page 26, lines 23-28 wherein Applicants teach whether a compound fits into the catalytic domain.
> 4) Page 27, lines 3-9 wherein Applicants describe how one can identify a potential inhibitor of Tie-2 based on the ability of one or more functional groups of the compounds, when present in the Tie-2 catalytic domain, to interact with one or more subsites of the Tie-2 catalytic domain.
>
> The instant specification teaches crystallization conditions for diphosphorylated Tie-2 802-1124 on page 48, Tie-2 (D964N) 802-1124 (SEQ ID NO 1) on page 49 and for Tie-2 (D964N) 802-1124 (SEQ ID NO 2) on page 51 of the instant application. In Example 2, Applicants have exemplified the steps of claim 21 by identifying a compound which is an inhibitor of Tie-2 by obtaining the atomic coordinates of a crystal of a polypeptide comprising the catalytic domain of a Tie-2 protein, using these atomic coordinates to define the active subsites of Tie-2 and identifying a compound which binds to one or more active subsites and inhibit the Tie-2 protein. Applicants also teach inhibitor docking in Example 2.
> Further, in Examples 3 and 4, Applicants teach how to determine the in vitro potency of compounds in inhibiting Tie-2. Once a compound is found to bind to the active subsites, one can utilize the assays taught in the instant application to measure the ability of the compound to inhibit Tie-2. Applicants have taught all steps of claim 21 as well as how to evaluate the potency of compounds with respect to their ability to inhibit Tie-2.
> Therefore, Applicants conclude that claims 21-27, 32 and 33 are enabled.

These statements are deemed unpersuasive as one skilled in the art would not conclude that a compound that binds to an "active subsite or sites" is necessarily an inhibitor, since this compound could equally be an activator (agonist) or have no effect, depending on where and how it binds. Not all molecules that bind to enzymes are inhibitors. Not every ligand that binds to a receptor also activates the receptor. Instant claim 21 recites identifying a compound that binds to one or more active subsites, but this compound cannot be automatically assumed to be an inhibitor. One skilled in the art would need to have additional information, such as information regarding which residues of the protein interact with known inhibitors or some other comparison of binding properties to known inhibitors. While the specification recites that compounds interact with one or more subsites within the catalytic domain of Tie-2 (page 26, last paragraph), this is not specifically recited in instant claim 21 that merely recites "binds to one or more active subsites". It is also noted on page 5, last paragraph, that identifying compounds that fit into the catalytic domain are *potential* inhibitors of Tie-2, not necessarily inhibitors. Applicants arguments are deemed unpersuasive for the reasons given above.

Conclusion

No claim is allowed.

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO

MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Papers related to this application may be submitted to Technical Center 1600 by facsimile transmission. Papers should be faxed to Technical Center 1600 via the PTO Fax Center. The faxing of such papers must conform with the notices published in the Official Gazette, 1096 OG 30 (November 15, 1988), 1156 OG 61 (November 16, 1993), and 1157 OG 94 (December 28, 1993) (See 37 CFR §1.6(d)). The Central Fax Center number for official correspondence is (571) 273-8300.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Carolyn Smith, whose telephone number is (571) 272-0721. The examiner can normally be reached Monday through Thursday from 8 A.M. to 6:30 P.M.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ram Shukla, can be reached on (571) 272-0735.

June 21, 2007

/Carolyn Smith/
Primary Examiner
AU 1631